Back pain as a first symptom of hematologic malignancy in a 9-year-old girl

Ból pleców jako początkowy objaw choroby rozrostowej układu krwiotwórczego u 9-letniej dziewczynki

Aneta Szudy, Jakub Litak, Joanna Zawitkowska, Jerzy Kowalczyk

ABSTRACT

Described case involves 9-year-old, otherwise healthy girl, which was admitted to a local hospital due to acute back pain persisting for a couple of days. Pain appeared suddenly, without any preceding trauma, and was accompanied by fever. Physical examination was normal apart from forced, defensive back flexion. Initial laboratory tests showed elevated inflammatory markers without any additional changes in blood cell count. Patient was transferred to Rheumatology Department of Children's Clinical Hospital in Lublin, Poland for further diagnosis and treatment. Extensive diagnostic procedures were performed, including bone scan, MRI of the spinal column and multiple laboratory tests. Pain and fever persisted despite intensive anti-inflammatory and antibiotic therapy. Changes in blood morphology led to extended oncological diagnostics. Eventually patient was diagnosed as having acute lymphoblastic leukemia (pre-B ALL).

Keywords: pre-B ALL, acute lymphoblastic leucemia, acute back pain, musculosceletal symptoms, malignancy, fever

STRESZCZENIE

Opisany przypadek dotyczy dziewięcioletniej, dotychczas zdrowej dziewczynki, która z powodu utrzymującego się od kilku dni ostrego bólu pleców i gorączki trafiła do szpitala terenowego. Dolegliwości bólowe wystąpiły nagle, bez żadnego poprzedzającego je urazu, towarzyszyła im podwyższona temperatura ciała. W badaniu fizykalnym oprócz przymusowego, obronnego zgięcia kręgosłupa nie stwierdzono nieprawidłowości. Wyniki wstępnych badań wykazały wysoki poziom markerów stanu zapalnego bez dodatkowych odchyleń w obrazie morfologii krwi. Pacjentkę skierowano do Kliniki Reumatologii i Chorób Tkanki Łącznej celem rozszerzenia diagnostyki i leczenia. Wykonano badania obrazowe: scyntygrafię kości, badanie rezonansu magnetycznego kręgosłupa, a także szereg badań laboratoryjnych. Ból i gorączka utrzymywały się dalej, mimo zastosowanego intensywnego leczenia przeciwzapalnego i antybiotykoterapii. Zaburzenia w obrazie morfologii krwi stały się powodem wdrożenia diagnostyki onkologicznej. Ostatecznie u dziewczynki rozpoznano ostrą białaczkę limfoblastyczną (pre-B ALL).

Słowa kluczowe: ostra białaczka limfoblastyczna, dzieci, bóle pleców, bóle kości, objawy mięśniowo-szkieletowe, objawy reumatologiczne, nowotwory

Pediatr Pol 2012; 87(1): 95–98

Otrzymano/Received: 15.10.2011
Zaakceptowano do druku/Accepted: 7.11.2011

Klinika Hematologii, Onkologii i Transplantologii Dziecięcej
Dziecięcy Szpital Kliniczny im prof. Antoniego Gębali w Lublinie

Konflikt interesu/
Conflicts of interest:
Autorzy pracy nie zgłaszają konfliktu interesów

Adres do korespondencji/
Address for correspondence:
Aneta Szudy
Klinika Hematologii, Onkologii i Transplantologii Dziecięcej Dziecięcego Szpitala Klinicznego im. prof. Antoniego Gębali w Lublinie
ul. Chodźki 2
20-093 Lublin
Tel: 81 71 85 1 01
Fax: 81 743 13 80
e-mail: anetaszudy@gmail.com

Case presentation. 9-year-old, otherwise healthy girl, presented to a local hospitals with acute back pain and fever persisting for a couple of days. Symptoms appeared suddenly, and weren't associated with any preceding trauma. If restricted the ability to move freely and made breathing difficult. Complaints were intensified especially during the night, and were waking the child from her sleep. The symptoms did not alleviate after administration of non-steroid anti inflammatory drugs (NSAID's).

On admission patient presented forced, defensive back flexion and restriction of respiratory movements. Joints have not showed any signs of oedema or pain. Vital signs: temperature 37.5°C, heart rate 125/min, blood pressure 120/70, ECG were normal. Blood examination showed moderate anemia, WBC and platelets were normal. Tests results were: HGB 10.8 g/dl, RBC 3.68*10^6/µl, HCT 29.8%, PLT 161*10^3/µl, WBC 6.7*10^3/µl including: neutrophile 42%, limphocytes 53%, monocytes 2%, eozynophiles 2%, basophiles 1%. Elevated inflammatory markers were noted: ESR was 110 mm/h and CRP 48 mg. Urinalysis was normal. Chest X-ray revealed scoliosis in the thoracic spine. Patient was started on Paracetamol and antybiotic – Cefotaksym (3rd generation cephalosporin), without clinical effect.

Patient was transferred to Rheumatology Department of Children's Clinical Hospital in Lublin, Poland for further diagnosis and treatment.

HLA B27 was tested negative. Biochemical tests showed: normal level of hepatic enzymes (AlAT 11U/l, AspAT 19 U/l), alkaline phosphatase 189.24 U/l, acid phosphatase 9.55 U/l, creatinine 0.6 mg/dl, uric acid 4.1 mg/dl, elevated D-dimers 3739 µg/l, elevated LDH 350 U/l, CRP 2.4 mg/l and elevated ESR of 45 mm/h.

Serology showed: antibodies in the IgG class 1028.49 mg/dl, IgM 66.42 mg/dl, elevated levels of antybodies against Mycoplasma pneumoniae in both IgM and IgG classes and against Parvo B19 virus in the IgG class.

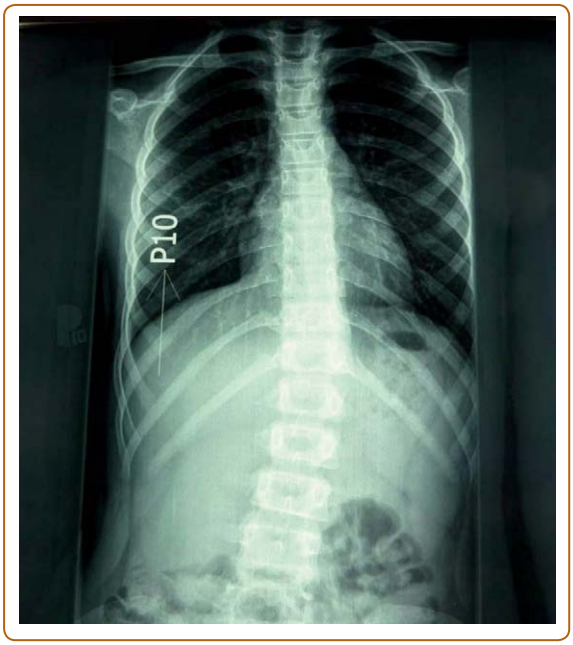

Fig. 1. AP projection CXR showing lateral flexion of the spine
Ryc. 1. RTG w położeniu AP ukazujący boczne zgięcie kręgosłupa

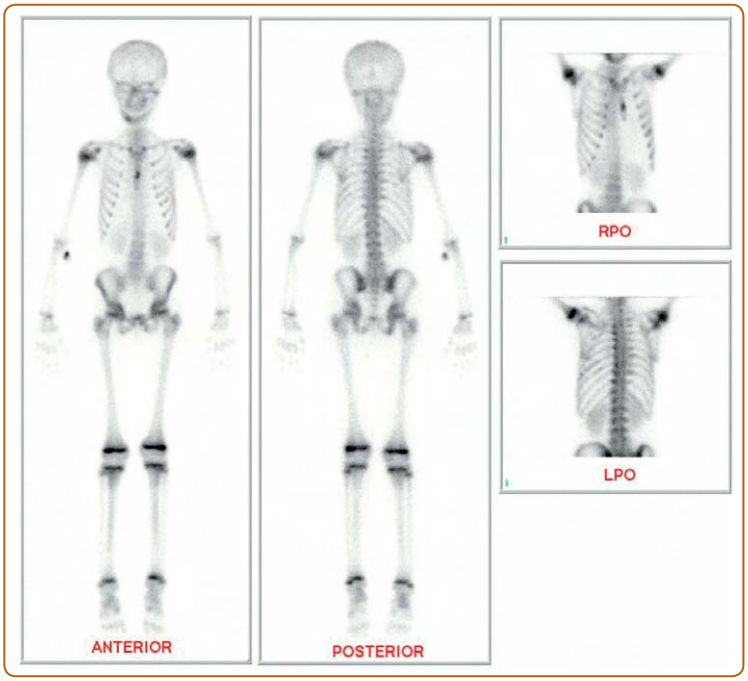

Fig. 2. Presence of increased metabolism area in sternums bone tissue; distribution of radioisotope in the ribs is uneven, with slight segmental increase in the radioactivity in the rear parts of the left VII and VIII ribs, and right VII, IX, XI ribs; focal increase in the accumulation of radioisotope on the right side of the mandible corresponds with the exchange of a milk tooth
Ryc. 2. Obecność powierzchni o zwiększonym metabolizmie tkanki kości mostka; dystrybucja izotopów w żebrach jest nierówna, z lekkim segmentowym wzrostem radioaktywności w tylnej części lewego VII i VIII żebra i prawego VII, IX, XI; ogniskowy wzrost akumulacji radioizotopu po prawej stronie żuchwy odpowiada wymianie zębów mlecznych

Aerobic and anaerobic blood cultures, swabs from the skin, throat and nose and urine cultures were all negative – no growth was noted.

Subsequent imaging was done: lateral CXR showed no interstitial changes or pleural effusion. X-Ray of the thoracic and lumbar spine revealed forced defensive flexion of the spine with the curvature pointing to the left on the Th12-L1 level (Fig. 1).

CT scan of the chest have not revealed any abnormalities, lungs had no focal lesions, mediastinum was not enlarged.

Ultrasound scan showed organs of normal size, with no abnormalities.

Bone scan revealed presence of singular changes, showing increased metabolism of bone tissue in sternum and ribs (Fig. 2).

MRI of the lumbar spine confirmed the presence of high signal foci within the VII and IX ribs on the right after the intravenous administration of paramagnetic. Changes were limited to the ribs (Fig. 3, 4).

Cefotaxime was used in combination with clarithromycin and analgesics: diclofenac and paracetamol. Despite the treatment girl's condition did not improve. Etiology of the disorder at this stage still remained unclear.

An interesting trend was found in the results of subsequent blood cell counts. They revealed a decreasing concentration of hemoglobin, RBC and platelet count. Finally, blasts become present in the peripheral blood (Tab. I).

These disorders have become a reason for starting the hematological diagnostics.

In the bone marrow biopsy the image was monotone, with very high amount of cells in the bone marrow matrix. 91.6% of cells were young, blastic, of medium size. Red blood cell aplasia, few granulocytes and megakariocytes. In the cytochemical tests, PAS reaction was positive in 82% of blasts, POX reaction in blastach was negative. Based on the tumor cell immunophenotype – expression of markers: Td T+, CD19+, CD 22+, CD45+, cIgM+ patient was diagnosed with acute lymphoblastic leukemia pre-B ALL. Cytogenetic study ruled out the presence of unfavorable prognostic fusion genes: BCR\ABL and MLL\AF4.

Based on the results the patient was stratified to the intermediate-risk group (IR) and started therapy according to the ALL IC 2002 Protocol.

The time from initial presentation to final diagnosis was nine weeks.

Currently the described girl is in good condition. Control bone marrow biopsy after completion of therapy shows the characteristics of haematologic remission, the results of the mielogram reveal 2.4% blasts.

Discussion

Typical clinical picture of hematologic proliferative disease in the form of pale skin and mucous membranes, weakness, fever, bruising, bleeding, bone pain, arthralgia, abdominal pain, or lymphadenopathy may mimic other diseases common in pediatrics [2]. Differential diagnosis of bone pain in children is very broad. Among the most common causes are: trauma, congenital defects, infections, rheumatologic diseases, but also malignancies. Alarming symptoms include acute, increasing pain, restriction of movement, accompanying neurologic symptoms and ailments persisting despite anti-inflammatory treatment [1, 3].

Findings reported in the literature and own observations indicate that symptoms associated with the musculoskeletal system in patients with acute lymphoblastic leukemia are not uncommon [3, 4, 7].

Among the 25 patients diagnosed with ALL and treated in the Department of Hematology Children Clinical Hospital in Lublin during the last year, 11 (i.e. about 45%) reported such symptoms. Pain of long bones was the dominant one, with children complaining mostly of pain in the lower limbs and large joints, knee and hip pain. Back pain affected only one, currently presented patient. In most cases, pain was accompanied by fever. Such patients often pose a significant diagnostic problem for physicians. Frequently, they received a non-steroidal anti-inflammatory drugs and antibiotics. Lack of clinical improvement and subsequent symptoms, including weakness, loss of appetite, and bruising on the skin led to blood tests, which often revealed a profound anemia, and severe thrombocytopenia.

It is not uncommon for patients with ALL with bone pain to be mistakenly diagnosed with osteomyelitis, bone or joint inflammation, which delays the correct diagnosis [5]. Jonsson et al. [6] in his study reviewed the records of 296 young patients with a diagnosis of All to determine the relationship between bone pain and the hematological abnormalities specific for acute lymphoblastic leukemia. The results: 22% patients had some bone pain and 18% had prominent bone pain that overshadowed other manifestations of the leukemia. He concluded that children with ALL who have prominent bone pain preceding the diagnosis frequently have nearly normal hematologic indexes and that may delay in diagnosis.

Skeletal lesions that can occur in a child with ALL include extensive osteoporosis, periosteal new bone formation, osteolysis, osteosclerosis and permeative destruction [8]. Frequently, the lesions are located in long bones. Back pain affects really rare in childhood leukemia. There are only a few published cases of patients with ALL, in whom back pain was the main symptom. Beckers et al. [9] reported a case of boy with 3-month history of back pain; laboratory findings were nearly normal but subsequent imaging revealed presence of extensive osteoporosis and vertebral collapses. Hafiz et al. [10] described a case

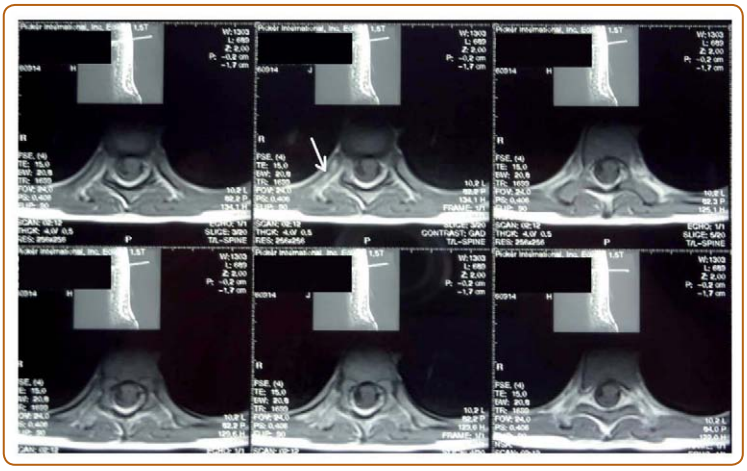

Fig. 3. Hyperintense changes within the ribs
Ryc. 3. Hiperintensywne zmiany w żebrach

Fig. 4. Lateral projection of the spine, with no pathological changes
Ryc. 4. Boczne projekcje kręgosłupa bez zmian patologicznych

Table I. Evolution of hematological changes
Tabela I. Ewolucja zmian hematologicznych

	WBC k/ul	RBC M/ul	Hb g/dl	MCV fl	PLT K/ul	Lym %	Segm %	Blast %
27.10	5.1	3.7	10.7	82.1	175	63.9	31.7	0
3.11	5.3	3.5	10	84.6	257	65.4	30.8	0
12.11	4.5	3.4	9.8	84.5	161	66.4	26.2	0
18.11	5.99	3,1	8.8	84.4	160	56.2	26	14

of child with 2-month history of back pain and vertebral compression fractures and also without the hematological findings specific for leukemia.

Summary

Described patient presented with atypical symptoms and no change in blood counts, which contributed to the 9-weeks delay in diagnosis. Differentiating rheumatic from malignant causes of musculoskeletal symptoms is difficult because early symptoms are often very similar. Abnormalities in complete blood counts don't have to be present. Leukaemia should be always considered in the initial differential diagnosis of unexplained osteoarticular complaints in children [11, 12].

Although rare, ta back pain may be the first and only sign of malignancy.

References

1. Marin JR. A teenage girl with acute back pain. Clinical Pediatric Emergency Medicine, 2007; 8(1): 65–68.
2. Niedźwiecki M, Płoszyńska A, Maciejka-Kapuścińska L, Balcerska A. Maski kliniczne chorób rozrostowych układu krwiotwórczego u dzieci – prezentacja przypadków. Forum Medycyny Rodzinnej, 2009; 3(2): 143–153.
3. Ćwiklińska M, Balwierz W. Osteoarticular pains as early manifestation of malignancies in children. Przegląd Lekarski, 2009; 66(1\2): 39–44.
4. Postępski J, Majcher A, Opoka-Winiarska W, Stefaniak J, Kostrzewa M. Reumatological symptoms masking neoplasm in children. Wiadomości Lekarskie, 2007; 60(9\10): 422–428.
5. Wieczorek M, Sońta-Jakimczyk D, Bubała H, Szczepański T, Hicke-Roberts A. The osteoarthralgic symptoms preceding acute lymphoblastic leukemia. Wiadomości Lekarskie, 1998; 51(Suppl. 4): 296–299.
6. Jonsson OG, Sartain P, Ducore JM, Buchman GR. Bone pain as an initial symptom of childhood leukemia: association with nearly normal hematologic indexes. Journal of Pediatrics, 1990; 117: 233–7.
7. Casado PR, Barrios LM, de Inocencio AJ, Baro FM, Vivanco MJL. Muskuloskeletal pain: a common initial sign of acute lymphoblastic leukaemia. An Pediatr (Barc), 2010; 72(6): 428–31.
8. Gallagher DJ, Phillips DJ, Heinrich SD. Orthopedic manifestations of acute pediatric leukemia. Orthop Clin North Am, 1996; 27 (3): 635–44.
9. Beckers R, Uyttebroeck A, Demaerel P. Acute lymphoblastic leukaemia presenting with low back pain. Eur J Paediatr Neurol, 2002; 6(5): 285–287.
10. Hafiz MG, Islam A, Siddique R. Back pain and vertebral compression: an unusual presetation of childhood acute lymphoblastic leukemia. Mymensingh Med J, 2010; 19(1): 130–136.
11. Murray MJ, Tang T, Ryder C, Mabin D, Nicholson JC. Childhood leukaemia masquearading as juvenile idiopathic arthritis. BMJ, 2004; 329(7472): 959–61.
12. Bradlow A, Barton C. Arthritic presentation of childhood leukaemia. Postgrad Med J, 1991; (67): 562–64.